Biomedical Science

Indoor Radon and Lung Cancer
Estimating the Risks

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Radon is ubiquitous in indoor environments. Epidemiologic studies of underground miners with exposure to radon and experimental evidence have established that radon causes lung cancer. The finding that this naturally occurring carcinogen is present in the air of homes and other buildings has raised concern about the lung cancer risk to the general population from radon. I review current approaches for assessing the risk of indoor radon, emphasizing the extrapolation of the risks for miners to the general population. Although uncertainties are inherent in this risk assessment, the present evidence warrants identifying homes that have unacceptably high concentrations.

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Radon, a naturally occurring radioactive gas in the decay series of uranium 238 (Figure 1), is ubiquitous in indoor environments.[1] Radon is also present in the air of underground mines where it is released from ore or transported into the mine in water. More than 100 years ago, miners of metal ore in Schneeberg, Germany, were found to be at risk for lung cancer.[2] Early in the 20th century, high levels of radon were measured in the Schneeberg mines and in nearby mines in Jáchymov (Joachimstal), Czechoslovakia, where high lung cancer rates were also noted; the radon was hypothesized to be a possible cause of the high rates of lung cancer in the miners. Subsequent epidemiologic studies of other populations of underground miners have provided strong and consistent evidence that radon causes lung cancer through damage to target cells in the tracheobronchial epithelium. The damage is inflicted by the α-particles released by short-lived radon progeny (Figure 1).[3]

The presence of radon in indoor air was documented as early as the 1950s.[4] Beginning in the 1970s, research was initiated to address sources of indoor radon, determinants of concentration, health effects, and approaches to mitigation. In the United States, the problem of indoor radon received widespread publicity and intensified investigation after a widely publicized incident in 1984. During routine monitoring at a Pennsylvania nuclear power plant, a worker was found to be contaminated with radioactivity. A high concentration of radon in his home was subsequently identified as responsible for the contamination. High levels of radon have now been documented in homes in the region of the Northeast where this worker lived and in many other locations throughout the United States.

In the US, concentrations of radon in homes are generally expressed in units of picocuries (pCi) per liter. For historic reasons, the concentration of radon progeny in mines has been expressed as Working Levels (WL), a unit based on the α-particle energy of the mixture of radon progeny.[5] Under the conditions of radioactive equilibrium between radon and its progeny, assumed to typically prevail in a home, 1 pCi per liter is equivalent to about 0.005 WL. Exposure to radon progeny is measured as Working Level Months (WLM), with exposure at 1 WL for 170 hours, the approximate number of hours worked monthly, yielding 1 WLM. Because most persons spend more than 170 hours per month at home, a concentration of 1 WL in a home typically yields an exposure greater than 1 WLM monthly. In other countries, these units of concentration and exposure have been replaced by the Système International (SI) units. In SI units, the concentration of radon in air is expressed as becquerels per cubic meter (Bq per m^3), where 37 Bq per m^3 equals 1 pCi per liter. Cumulative exposure in SI units is expressed in joule-hours per cubic meter (Jh per m^3), and 1 WLM is 3.5×10^{-3} Jh per m^3.

Measurements made in the surveys of states conducted by the US Environmental Protection Agency (EPA) and in other studies have shown that the distribution of radon concentrations indoors is approximately log normal, with a mean concentration of about 1 to 1.5 pCi per liter in living areas (Figure 2).[6] Many homes have concentrations well above the average, even exceeding occupational standards set for underground mines. Two features of this distribution merit consideration in judging the public health risk posed by radon. First, the population's average exposure largely reflects the contribution of time spent in homes with lower concentrations; thus, the burden of lung cancer attributable to indoor radon predominantly results from lower levels of exposure.[7] Second, the number of homes considered as possibly having unacceptable concentrations varies markedly with the selected limit for acceptability. As the value for the limit drops below 4 pCi per liter, the number of homes exceeding the acceptable concentration increases rapidly.

The development of national policy for indoor radon, or other indoor pollutants of health concern, should be based on an understanding of the population's pattern of exposure, the risks of disease associated with exposure, the capability of accurately measuring exposure, the availability of effective techniques for preventing and mitigating exposure, and the costs of managing the risks of exposure. The technique of quantitative risk assessment has an increasingly prominent

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ABBREVIATIONS USED IN TEXT

BEIR IV = [Committee on] Biological Effects of Ionizing Radiation IV
EPA = Environmental Protection Agency
SI = Système International
WL = Working Level
WLM = Working Level Months

role in gauging the extent of a hazard as a basis for policy development.[8] In the United States, although the EPA does not have statutory authority to regulate directly the concentrations of radon in the air of homes, it has, through its Radon Program, taken the lead in developing policy. The EPA promulgates action guidelines for acceptable concentrations indoors and also advises concerning techniques for measuring, preventing, and mitigating high concentrations of indoor radon. The pamphlet, "A Citizen's Guide to Radon," sets out the EPA's approach to measurement and control and provides action guidelines for concentrations requiring a specific response.[9] The agency encourages testing nearly all homes as a basis for controlling indoor radon. The "Citizen's Guide" is currently undergoing revision.

Assessing the Risks of Indoor Radon

Three distinct approaches merit consideration as being potentially informative for estimating the risks of indoor radon:

- A deterministic model is used that directly links concentration to carcinogenic response, based on a full understanding of the biologic basis of carcinogenesis by radon progeny;
- Risk estimates are developed from epidemiologic investigation of indoor radon and lung cancer; and
- Risks observed in underground miners with exposure to radon are extrapolated to the general population.

The first approach, using a comprehensive biologic model, cannot yet be implemented with sufficient confidence in the results because of gaps in our understanding of carcinogenesis by radon progeny. With regard to the second approach, many epidemiologic studies using the case-control design are presently being conducted to estimate directly the lung cancer risks of indoor radon.[10] Because most of these studies are not yet completed, the third option, extrapolating from the studies of miners to the general population, has served as the principal approach for assessing the risk of indoor radon exposure.[3,11]

Model-Based Approaches

Model-based approaches have been applied in the past to estimate the risks of lung cancer associated with exposure to radon progeny. Using mathematic representations of the respiratory tract, the dose of α-particle energy delivered to target cells in the respiratory tract can be estimated.[3] By combining the dose estimates with risk coefficients describing the increased risk per unit of a biologically effective dose, risk projections can be made. This approach is subject to many uncertainties, and it has been rejected by recent expert panels in favor of risk estimation using the data from studies of miners.[3] As the understanding of carcinogenesis by radon progeny advances, it may become possible to develop more biologically accurate models that offer more confident risk projections. Research supported by the US Department of Energy and other agencies has this goal.

Epidemiologic Approach

After the problem of indoor radon was recognized, lung cancer mortality or incidence rates for geographic areas,

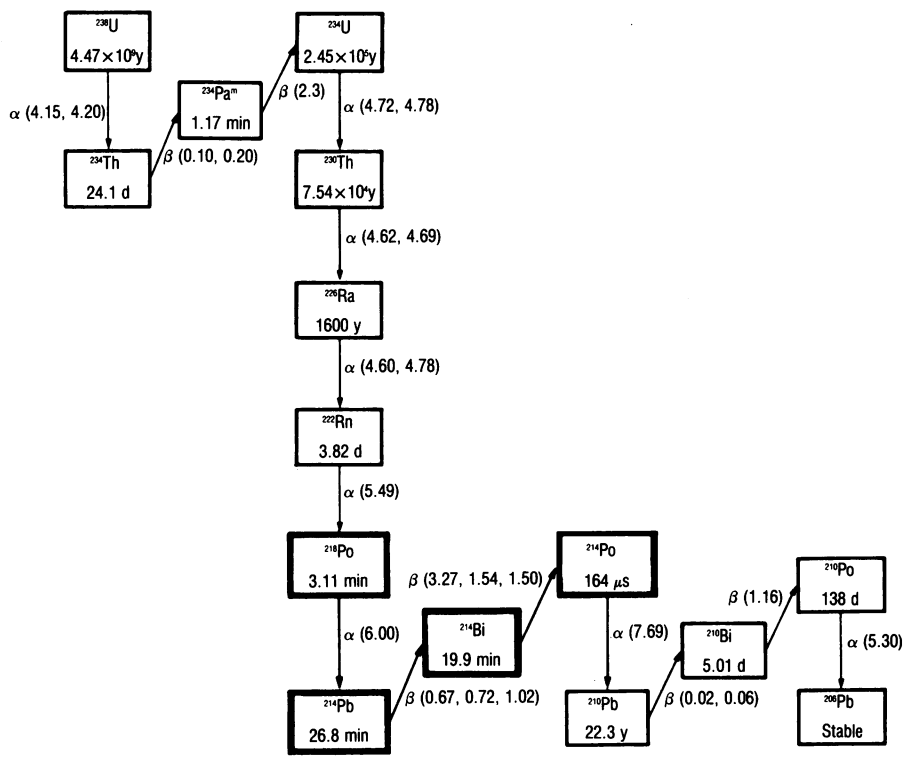

Figure 1.—The principal decay pathway is shown for uranium 238. Short-lived radon progeny are indicated by bold outline (modified from Figure 1-2 in Nero[1]; reprinted with permission).

such as counties, were correlated with estimated radon concentrations for these units. This type of epidemiologic investigation, termed an "ecologic" study, has well-described limitations.[12] The results of ecologic studies are potentially limited by uncertainties in estimating exposure, an inadequate control of factors confounding and modifying the relation of radon with lung cancer such as cigarette smoking, and biologically inappropriate assumptions that may be implicit in the statistical methods used to analyze the data.[13] Thus, although many ecologic studies have shown a positive correlation of estimated indoor radon concentration and lung cancer rates, the results are not informative for estimating the risk of lung cancer associated with indoor radon concentrations. Several studies showing either a lack of association of radon concentration with lung cancer rates, or even a negative association, have received widespread media attention.[14] The incongruity of these findings with the assumed carcinogenicity of indoor radon has been emphasized by critics of programs to control radon,[15] although the negative studies share the limitations of the positive studies. Moreover, the findings of these purportedly negative ecologic studies are inconsistent with the strong evidence from epidemiologic studies of miners and from studies of animals and with present concepts of carcinogenesis by α-particles.

The risks of indoor radon are being assessed in epidemiologic studies using the case-control design; estimated exposures of lung cancer cases to radon are compared with exposures of control subjects not having lung cancer.[16] Case-control studies of indoor radon and lung cancer have already been reported, some showing no association of radon exposure with lung cancer risk, and others showing exposure-response relations compatible with those observed in the studies of underground miners.[11,17,18] Worldwide, 15 or more case-control studies are in progress or are planned.[10]

Case-control studies of any disease have well-characterized limitations that reflect the difficulty of obtaining accurate information on exposures of concern, selecting the control series, correctly classifying cases, and controlling for relevant confounding and modifying factors. Estimating exposure is particularly problematic for case-control studies of indoor radon and lung cancer. Exposure occurs throughout the lifetime of a subject, and most persons have lived in many dwellings during their lives. To estimate exposures in the

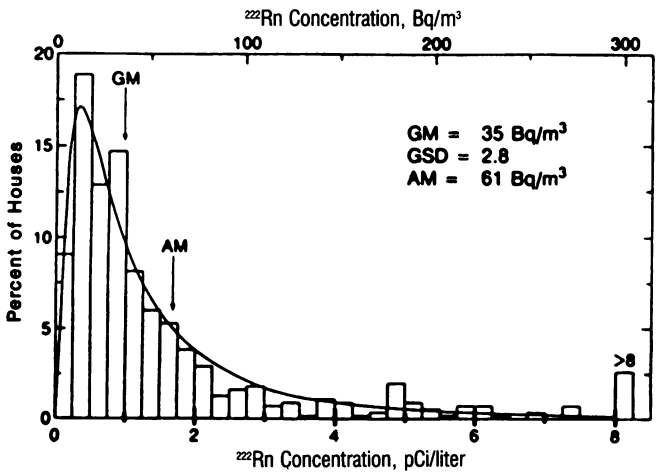

Figure 2.—The probability distribution of radon 222 in US homes is given, based on 19 data sets that include 552 homes (from Nero[1]). AM = arithmetic mean, GM = geometric mean, GSD = geometric standard deviation

TABLE 1.—*Sample Size Requirements in a Lung Cancer Case-Control Study to Detect a Trend in Risk With Radon Exposure; Effects of Radon Measurement Error and Population Mobility**

Measurement Error, %	Mobility Pattern: 1 Residence, 60 yrs	Mobility Pattern: 6 residences, 10 yrs each
None	251	1,446
30	288	2,303
50	365	4,059
100	973	18,032
150	4,186	91,875
200	29,542	674,540

*Number of cases is shown in a hypothetical study with 2 controls per case designed to reject the null hypothesis of no trend with exposure, assuming the true increment is 1.5% per Working Level Month (from Lubin et al [Table 5][16]).

context of a case-control study, a subject's current and former residences are identified, and radon concentrations are measured; it is assumed that current concentrations reflect those during the period a person resided in the residence. This retrospective estimation is subject to diverse sources of uncertainty, and feasibility may be compromised by the difficulty of identifying and gaining access to all previous residences. Moreover, the measuring devices themselves have inherent error.

Lubin and co-workers assessed sample size needs for case-control studies of radon.[16] Their analysis showed that large sample sizes are needed to have adequate statistical power for addressing the scientific hypotheses inherent in the information needs of policymakers (Table 1). For example, Table 1 shows the number of cases needed to identify a statistically significant trend of lung cancer risk with radon, comparable to the value observed in the studies of miners, as the degree of error in measuring radon and population mobility increases. Population mobility reduces the variation of exposures and thereby necessitates larger sample sizes. Similarly, increasing measurement error also increases sample size needs. Because of the complexity of estimating lifetime exposure to radon, it is likely that the measurement error is at least 50% or even higher.[16] These sample size calculations suggest that individual studies will not provide sufficiently informative answers to guide the evolution of policy on indoor radon.

Because of the limited informativeness of the individual studies, the pooling of results using meta-analysis techniques has been proposed.[10] An international effort is in progress to link the results of the case-control studies now under way.

Estimating Risk Using the Studies of Underground Miners

The risk of lung cancer associated with exposure to radon decay products has been investigated in about 20 different populations of underground miners (Table 2). Almost all of these studies show a significant excess occurrence of lung cancer in comparison with the expected number of cases. About half of the studies include data on the exposures of individual miners to radon progeny; this detailed information is needed to estimate quantitatively the lung cancer risk associated with radon exposure.

To describe the increasing frequency of lung cancer with increasing exposure, statistical approaches are used to derive risk coefficients; these coefficients describe the increment in lung cancer risk per unit exposure to radon. The range of

TABLE 2.—*Populations of Underground Miners Included in Epidemiologic Investigations of Lung Cancer**

Substance Mined	Location of Study
Uranium	US: Colorado Plateau, New Mexico; Czechoslovakia; Canada: Ontario, Beaverlodge, Port Radium; Uranium Hill, Australia
Iron	Sweden: Kiruna, Grangesberg, Malmberget, Northern Sweden; England; France
Tin	Cornwall, England; Yunnan Province, People's Republic of China
Magnetite	Norway
Fluorspar	Newfoundland, Canada
Zinc-lead	Hammar, Sweden
Niobium	Norway

*From Samet [Table 2].[11]

coefficients characterizing the rise of excess relative risk with exposure is remarkably narrow among the reported investigations, spanning from 0.5 to 3.0 per 100 WLM.[11] A coefficient of 1 per 100 WLM (1% per WLM) implies that the lung cancer risk is doubled by a cumulative exposure of 100 WLM.

To estimate the risk of lung cancer associated with indoor radon, a risk coefficient derived from the studies of miners is used in a mathematic model to project the occurrence of cases of lung cancer caused by exposure. Such risk-projection models require explicit assumptions concerning the temporal expression of lung cancer risk after exposure and the effects of such potentially important factors as age at exposure, age at risk, and cigarette smoking. The two most widely applied risk-projection models are the relative risk and the attributable risk models; the relative risk model assumes that the background rate of lung cancer, which incorporates the effect of cigarette smoking, is multiplied by the risk from radon, whereas the attributable risk model assumes that the excess risk is additive to the background rate. Models incorporating time dependence of risk have also been described.

Diverse risk-projection models have been developed.[3,11] Because of differing underlying assumptions, the risk projections from these models may differ substantially.[11,19] For example, three models were published during the 1980s by agencies concerned with radiation risks, including the National Council for Radiation Protection and Measurements,[20] the International Commission on Radiological Protection,[21] and the National Research Council.[3] Projections of the incremental risk associated with exposure to 1 WLM are provided in Table 3. The percentages in the table describe the increment in risk from the radon progeny beyond the background risk for lung cancer. For example, the model of the National Research Council's Committee on the Biological Effects of Ionizing Radiation IV (BEIR IV) projects that exposure to 1 WLM at age 15 increases the lung cancer risk at age 35 years by 1.5% of the background risk of that age. A wide range of estimated risk is evident among the projections of the three models.

Extrapolation of Risk

In extrapolating risk from the studies of miners to the indoor environment, assumptions must be made concerning the relations between exposure to radon progeny and the dose of α-energy delivered to the respiratory tract in the two environments and other factors potentially modifying the carcinogenicity of radon progeny (Figure 3). Exposure-dose relations in the respiratory tract can be assessed using dosimetric models, which incorporate physical characteristics of the inhaled air and biologic features of the respiratory tract. In a recent report, another committee of the National Research Council assessed the comparative exposure-dose relations of radon progeny in the indoor and mining environments.[22] The committee's analysis suggested that exposure to radon progeny in the indoor environment was somewhat less potent in causing cancer than exposure in the mining environment. The committee's review identified other sources of uncertainty in using the data from underground miners, including a lack of information on exposure during infancy and childhood, the limitation of the studies of miners to men, little information on the combined effects of smoking and radon exposure, and incomplete information on the lifetime expression of the excess incidence of lung cancer associated with radon progeny exposure.

Although subject to uncertainties, the use of epidemiologic data from miners to estimate lung cancer risks from indoor radon indicates that indoor radon poses a substantial public health problem. Using the risk model developed by the BEIR IV Alpha Committee, Lubin and Boice estimated that about 13,300 lung cancer deaths annually are attributable to indoor radon exposure.[7] The EPA estimates radon risks by combining the BEIR IV model with the model developed by the International Commission on Radiological Protection and has attributed about 20,000 lung cancer deaths annually to indoor radon.[23] The new findings of the National Research Council's committee on comparative exposure-dose relations in homes and mines suggest that these estimates should be reduced by about 25%.[22] The EPA is currently revising its estimates.

Summary

Radon, a well-documented industrial cause of lung cancer in underground miners, is a ubiquitous indoor pollutant. Many homes have high radon concentrations, even in excess of the levels now permitted in underground mines. Extensive epidemiologic studies of underground miners, in addition to complementary investigations of animals, unquestionably establish the carcinogenicity of radon and provide a basis for estimating the risks of indoor radon. The resulting risk projections, about 10,000 to 20,000 cases of lung cancer annu-

TABLE 3.—*Increment in Lung Cancer Risk for 1 WLM at Age 15 or 35 Years Projected by 3 Models**

Increment (%) at Attained Age (yr)	Model			
	NCRPM†			
	Male	Female	ICRP‡	BEIR IV§
	Exposure at age 15 yr			
35	0	0	1.9	1.5
50	0.3	0.7	1.9	1.5
65	0.05	0.2	1.9	0.5
85	0.02	0.1	1.9	0.5
	Exposure at age 35 yr			
50	0.6	1.4	0.6	3.0
65	0.1	0.4	0.6	0.5
85	0.05	0.2	0.6	0.5

*From Samet (Table 8).[11]
†From the National Council on Radiation Protection and Measurements (NCRPM).[20]
‡From the International Commission on Radiological Protection (ICRP).[21]
§From the Committee on the Biological Effects of Ionizing Radiation IV Alpha (BEIR IV).[3]

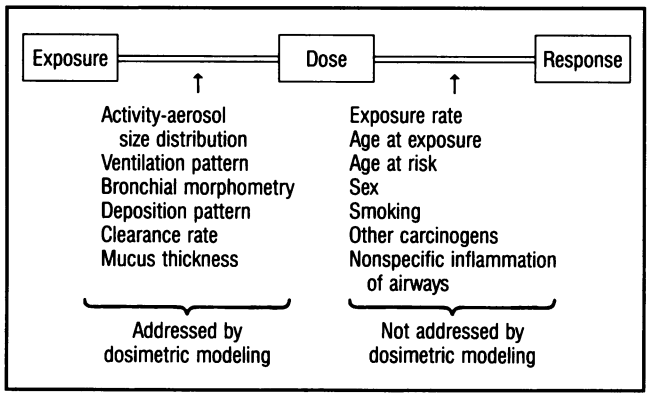

Figure 3.—Sources of uncertainty are shown in extrapolating radon risks from studies of miners to the general population exposed indoors (from the National Research Council[22]).

ally in the United States, indicate the significant public health problem posed by indoor radon.

Despite the extent of the evidence available, the risk posed by indoor radon has been questioned. Uncertainties in extrapolating data from miners to the general population and a failure to quickly confirm the hazard through epidemiologic studies are the most often cited arguments (Health Physics Society Newsletter, January 1991).[15] Ecologic studies, however, have substantial methodologic limitations for addressing indoor radon exposure, and even case-control studies may not be sufficient until their data are pooled. In the meantime, dosimetric analyses, as recently reported by the National Research Council's Committee, indicate that indoor radon delivers only a moderately lower dose of α-energy to the lung in comparison with exposure in mines. Thus, the present evidence warrants the conclusion that indoor radon should be considered a human carcinogen and justifies efforts to identify homes with unacceptably high concentrations. Research in progress can be expected to reduce uncertainties and provide more precise characterization of the risk of indoor radon.

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